

What is claimed is:

1. A method for producing a hepadnavirus virion that is infectious in vitro which comprises:

(a) introducing into a cell (i) a hepadnavirus genome expression vector and (ii) a foamy retrovirus envelope expression vector which comprises a nucleic acid encoding at least a fragment of a foamy virus envelope protein; and

(b) culturing the cell thereby producing hepadnavirus virions comprising at least a fragment of a foamy virus envelope protein, wherein the hepadnavirus virions are infectious in vitro.

2. The method of claim 1, wherein the hepadnavirus genome expression vector lacks a nucleic acid encoding a hepadnavirus envelope protein.

3. The method of claim 1, wherein the hepadnavirus genome expression vector comprises at least one gene from a hepadnavirus genome selected from the group consisting of: a wood chuck hepatitis virus (WHV) genome, a ground squirrel hepatitis (GSHV) virus genome, a duck hepatitis B virus (DHBV) genome, a snow goose hepatitis virus (SGHV) genome, and a human hepatitis B virus (HBV) genome.

4. The method of claim 3, wherein the hepadnavirus genome expression vector comprises a gene from a human hepatitis B virus (HBV) genome.

5. The method of claim 3, wherein the hepadnavirus genome expression vector further comprises an exogenous regulatory element.
6. The method of claim 5, wherein the exogenous regulatory element is a human cytomegalovirus immediate-early gene promoter/enhancer (CMV-IE).
7. The method of claim 1, wherein the foamy retrovirus envelope expression vector comprises at least a fragment of a gene from a foamy virus genome selected from the group consisting of: a simian foamy virus (SFV) genome, a feline foamy virus (FFV) genome, a bovine foamy virus (BFV) genome, a sea lion foamy virus (SLFV) genome, a hamster foamy virus (HaFV) genome, and a human foamy virus (HFV) genome.
8. The method of claim 7, wherein the gene encodes an envelope protein or a fragment thereof.
9. The method of claim 1, wherein the foamy retrovirus envelope expression vector comprises a gene or a fragment of a gene from a human foamy virus (HFV) genome.
10. The method of claim 9, wherein the gene or the fragment of the gene from a human foamy virus (HFV) genome encodes the gp130env envelope gene product or a fragment thereof.
11. The method of claim 1, wherein the cell is a mammalian cell.

12. The method of claim 1, wherein the cell is an avian cell.
13. The method of claim 12, wherein the avian cell is an avian hepatocyte.
14. The method of claim 11, wherein the mammalian cell is a human cell.
15. The method of claim 14, wherein the human cell is a human embryonic kidney cell.
16. The method of claim 11, wherein the mammalian cell is a 293 cell.
17. The method of claim 14, wherein the human cell is a human hepatoma cell.
18. The method of claim 17, wherein the human hepatoma cell is an HepG2 cell or an Huh7 cell.
19. A hepadnavirus virion that is infectious in vitro which comprises at least a fragment of a foamy retrovirus envelope protein.
20. The hepadnavirus virion of claim 19, wherein the hepadnavirus virion is isolated.
21. The hepadnavirus virion of claim 19, wherein the foamy retrovirus is selected from the group consisting of: a simian foamy virus (SFV), a feline foamy virus (FFV), a bovine foamy virus (BFV), a sea lion foamy virus

(SLFV), a hamster foamy virus (HaFV), and a human foamy virus (HFV).

5 22. The hepadnavirus virion of claim 19, wherein the hepadnavirus virion comprises a chimeric envelope protein which consists essentially of (i) a hepatitis B virus envelope protein domain and (ii) a foamy virus envelope protein domain.

10 23. The hepadnavirus virion of claim 19, wherein the hepadnavirus virion further comprises a nucleic acid isolated from a subject infected by a hepadnavirus.

15 24. The hepadnavirus virion of claim 23, wherein the nucleic acid isolated from the subject infected by hepadnavirus encodes a reverse transcriptase.

20 25. The hepadnavirus virion of claim 19, wherein the hepadnavirus further comprises an indicator nucleic acid.

26. A cell comprising the hepadnavirus virion of any one of claims 19 to 25.

25 27. The cell of claim 26, wherein the cell is a mammalian cell.

28. The cell of claim 27, wherein the mammalian cell is a 293 cell.

30 29. The cell of claim 27, wherein the mammalian cell is a human cell.

30. The cell of claim 29, wherein the human cell is a human kidney cell.

31. The cell of claim 29, wherein the human cell is a human hepatoma cell.

32. A method for determining susceptibility for an anti-hepadnavirus drug which comprises:

(a) introducing into a first cell:

(i) a hepadnavirus genome expression vector;

(ii) a nucleic acid encoding at least a fragment of a foamy retrovirus envelope protein, and

(iii) an indicator nucleic acid;

(b) culturing the first cell from step (a) so as to produce hepadnavirus virions;

(c) admixing the hepadnavirus virions produced in step (b) with a second cell, wherein the anti-hepadnavirus drug is present with the first cell or the second cell, or with the first and second cell,

(d) measuring the amount of detectable signal produced by the indicator nucleic acid in the second cell, wherein the amount of

detectable signal produced is dependent upon
hepadnavirus virion infection of the second
cell; and

(e) comparing the amount of signal measured in
step (d) with the amount signal measured in
the absence of the drug, wherein a decrease
in the amount of signal measured in the
presence of the drug indicates
susceptibility to the drug and wherein no
change in signal measured or an increase in
the amount of signal measured in the
presence of the drug indicates resistance to
the drug.

33. The method of claim 32, wherein the hepadnavirus
genome expression vector of step (a) further comprises
a nucleic acid derived from a patient infected with
hepadnavirus.

34. The method of claim 33, wherein the nucleic acid
derived from a patient infected with hepadnavirus
comprises at least a fragment of a human hepatitis B
virus (HBV) gene.

35. The method claim 34, wherein the gene is an HBV P
gene, an HCV C gene, an HBV X gene or an HBV S gene.

36. The method of claim 34, wherein the nucleic acid
derived from a patient infected with hepadnavirus
encodes reverse transcriptase.

37. The method of claim 32, wherein the second cell is a mammalian cell
38. The method of claim 32, wherein the second cell is an avian cell.
38. The method of claim 32, wherein the avian cell is an avian hepacyte.
40. The method of claim 37, wherein the mammalian cell is a human cell.
41. The method of claim 40, wherein the human cell is a human embryonic kidney cell.
41. The method of claim 37, wherein the mammalian cell is a 293 cell.
43. The method of claim 40, wherein the human cell is a human hepatoma cell.
44. The method of claim 43, wherein the human hepatoma cell is an HepG2 cell or an Huh7 cell.
45. The method of claim 32, wherein the foamy retrovirus is selected from the group consisting of: a simian foamy virus (SFV), a feline foamy virus (FFV), a bovine foamy virus (BFV), a sea lion foamy virus (SLFV), a hamster foamy virus (HaFV), and a human foamy virus (HFV).

46. The method of claim 32, wherein the nucleic acid of step (a) (i) encodes a gp130env envelope protein.

5 47. The method of claim 32, wherein the nucleic acid of step (a) (i) encodes a chimeric envelope protein which consists essentially of (i) a hepatitis B virus envelope protein domain and (ii) a foamy virus envelope protein domain.

10 48. The method of claim 32, wherein the second cell expresses on its surface a protein which binds human foamy virus envelope protein.

15 49. A method for determining replication capacity of a hepadnavirus from an infected patient comprising:

(a) introducing into a first cell:

(i) a hepadnavirus genome expression vector;

20 (ii) a nucleic acid encoding at least a fragment of a foamy retrovirus envelope protein, and

(iii) an indicator nucleic acid;

25 (b) culturing the cell from (a) so as to produce hepadnavirus virions;

(c) admixing the hepadnavirus virions produced in step (b) with a second cell,

30 (d) measuring the amount of detectable signal produced by the indicator nucleic acid in the second cell, wherein the amount of detectable

signal produced is dependent upon hepadnavirus
virion infection of the second cell;

(e) normalizing the measurement of step (d); and

(f) comparing the normalized measurement of step (e)
with the amount signal measured when steps (a)
through (d) are carried out with a control
reference hepadnavirus, wherein an increase in
signal compared to the control indicates an
increased replication capacity and a decrease in
signal measured compared to the control indicates
a decreased replication capacity of the
hepadnavirus from the infected patient.

50. A method for determining susceptibility for an anti-
hepadnavirus drug which comprises:

(a) introducing into a cell:

- (i) a hepadnavirus genome expression vector;
- (ii) a nucleic acid encoding at least a
fragment of a foamy retrovirus envelope
protein, and

(iii) an indicator nucleic acid;

(b) culturing the cell from step (a);

(c) contacting the cell with the anti-hepadnavirus
drug;

(d) measuring the amount of detectable signal produced by the indicator nucleic acid in the cell; and

(e) comparing the amount of signal measured in step (d) with the amount signal measured in the absence of the drug, wherein a decrease in the amount of signal measured in the presence of the drug indicates susceptibility to the drug and wherein no change in signal measured or an increase in the amount of signal measured in the presence of the drug indicates resistance to the drug.

51. The method of claim 50, wherein wherein the hepadnavirus genome expression vector of step (a) further comprises a nucleic acid derived from a patient infected with hepadnavirus.

52. The method of claim 51, wherein the nucleic acid derived from a patient infected with hepadnavirus comprises at least a fragment of a human hepatitis B virus (HBV) gene.

53. The method of claim 52, wherein the gene is an HBV P gene or an HBV C gene.

54. A method for identifying a mutation in a hepadnavirus nucleic acid that confers resistance to an anti-hepadnavirus drug which comprises:

(a) sequencing the hepadnavirus nucleic acid prior to use of the anti-hepadnavirus drug;

(b) measuring susceptibility of the hepadnavirus sequenced in step (a) to the drug according to the method of claim 50;

(c) exposing the hepadnavirus to the drug so as to produce a decrease in the susceptibility of the hepadnavirus to the drug measured in step (b);

(d) comparing the sequence determined in step (a) with the sequence of the hepadnavirus following the exposure to the drug of step (c) so as to identify a mutation in the hepadnavirus nucleic acid that confers resistance to the anti-hepadnavirus drug.

55. The method of claim 54, wherein measuring step (b) comprises measuring susceptibility of the hepadnavirus sequenced in step (a) to the anti-hepadnavirus drug according to the method of claim 32.